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EXAMINER	
RAGHU, GANAPATHIRAM	
ART UNIT	**PAPER NUMBER**
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/802,034	PATEL ET AL.	
	Examiner	Art Unit	
	Ganapathirama Raghu	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *12 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5 and 39-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5 and 39-58* is/are rejected.

7)☒ Claim(s) *52 and 53* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/25/05; 9/12/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election without traverse of Group I, claims 5, and 39-58 for prosecution in their response dated 01/12/2007 is acknowledged. Claims 5 and 39-58 are pending in this application and are now under consideration for examination. Applicants' in their response to restriction/election have canceled claims 1-4, 6-38 and 59-63.

Priority

The priority date of 03/21/2003 granted for the instant claims is, the filing date of provisional application 60/456,245.

Drawings

Drawings are accepted for examination purposes only.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 06/25/2004 and 09/12/2005 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner is considering the IDS statement.

Claim Objections

Claims 52 and 53 are objected to because of the following informalities:

Applicant is advised that should claim 52 be found allowable, claim 53 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections: 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 50 and dependent claims 52-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 50, 52, 53 and 55 recite the phrase "*gumD-gumG*". It is not clear to the examiner as to what the phrase "*gumD-gumG*" means in the context of the above claims. Xanthan gum biosynthetic genes/operon comprises genes *gumB, C, D, E, F, G, H, I, J, K, L and M.* Does "*gumD-gumG*" also include *gumE* and *F* or *gumD* and *G* alone? Clarification is required. For examination purposes "*gumD-gumG*" is treated as comprising the genes *gumD, E, F* and *G*.

Claim Rejections: 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 5 and 39-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling for a method of producing a xanthan composition comprising a population of xanthan molecules having certain molecular length and increased viscosity relative to the xanthan produced by a wild-type strain, wherein said method comprises selectively increasing the amount of wild-type gene product of *gumB* and *gumC* (*gumB:XCC2454*; *gumC:XCC2453*, page 8 of specification) by a plasmid comprising said genes, but not genes

encoding *orfX* or *gumD, E, F* and *G*, in a mutant *Xanthomonas campestris* 2895 culture lacking wild-type *gum* genes (page 7 of specification) and precipitating said high viscosity xanthan preparation. However the specification does not reasonably provide enablement for a method of producing xanthan composition comprising a population of xanthan molecules having certain molecular length and increased viscosity relative to the xanthan produced by wild-type strain, wherein said method comprises selectively increasing the amount of any variant or mutant gene product of *gumB* and *gumC* by a plasmid comprising said genes but not genes encoding *orfX* or *gumD, E, F* and *G* in any strain of *Xanthomonas campestris* culture and precipitating said high viscosity xanthan preparation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claim.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 5 and 39-58 are so broad as to encompass any method of producing a xanthan composition comprising a population of xanthan molecules having certain molecular length and increased viscosity relative to the xanthan produced by wild-type strain, wherein said method comprises selectively increasing the amount of any variant or mutant gene product of *gumB* and *gumC* by a plasmid comprising said genes but not genes encoding *orfX* or *gumD, E, F* and *G* in

any strain of *Xanthomonas campestris* culture and precipitating said high viscosity xanthan preparation. The scope of the claims are not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides i. e., variant and mutants of *gumB* and *gumC* to be used in a method for producing xanthan of desired molecular length and viscosity. Since the amino acid sequence of a protein encoded by a polynucleotide determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires knowledge and guidance with regard to which amino acids in the protein's sequence and the respective codons in its polynucleotide, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the encoded proteins' structure relates to its function. In this case the disclosure is limited to a method of producing xanthan composition comprising a population of xanthan molecule having certain molecular length and increased viscosity relative to the xanthan produced by a wild-type strain, wherein said method comprises selectively increasing the amount of wild-type gene product of *gumB* and *gumC* (wild-type gene accession # *gumB: XCC2454* and wild-type *gumC* gene accession # *XCC2453*, page 8, Table 1 of specification) by a plasmid comprising said genes but not genes encoding *orfX* or *gumD, E, F* and *G* in a mutant *Xanthomonas campestris* 2895 culture lacking wild-type *gum* genes (page 7 of specification) and precipitating said high viscosity xanthan preparation. But the specification provides no guidance with regard to using variants, mutants of *gumB* and *gumC* i. e., for a method of producing xanthan composition comprising a population of xanthan molecules having certain molecular length and increased viscosity relative to the xanthan produced by wild-type strain, wherein said method comprises selectively increasing the

amount of any variant or mutant gene product of *gumB* and *gumC* by a plasmid comprising said genes but not genes encoding *orfX* or *gumD, E, F* and *G* in any strain of *Xanthomonas campestris* culture and precipitating said high viscosity xanthan preparation. In view of the great breadth of the claims, the amount of experimentation required to determine a use for the full scope of the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Whisstock et al., Q Rev Biophys. 2003 Aug; 36(3): 307-340), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to make and use the full scope of the polypeptides encompassed by these claims.

While enzyme isolation techniques and recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable (e.g., see Whisstock et al., Q Rev Biophys. 2003 Aug; 36(3): 307-340). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions or deletions.

The specification does not support the broad scope of the claims which encompasses a method of producing xanthan composition comprising a population of xanthan molecules having certain molecular length and increased viscosity relative to the xanthan produced by wild-type strain, wherein said method comprises selectively increasing the amount of any variant or mutant

gene product of *gumB* and *gumC* by a plasmid comprising said genes but not genes encoding *orfX* or *gumD, E, F* and *G* in any strain of *Xanthomonas campestris* culture and precipitating said high viscosity xanthan preparation, because the specification does not establish: **(A)** the structure of all polypeptides and the encoding polynucleotides, with desired *gumB* and *gumC* activity including variants and mutants; **(B)** regions of the protein/polynucleotide structure which may be modified without affecting the activity of encoded polypeptide; **(C)** the general tolerance of the polypeptide and the encoding polynucleotide to modification and extent of such tolerance; **(D)** a rational and predictable scheme for modifying any amino acid residue or the respective codon in the polynucleotide with an expectation of obtaining the desired biological function; **(E)** any strain of *Xanthomonas campestris* culture i. e., under any cellular context/any strain of *Xanthomonas campestris* culture, that can be used to produce the desired xanthan molecules, as the activity of mutant/variant genes would not yield a xanthan molecule with desired properties; and **(F)** the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to use the claimed invention in a manner reasonably correlated with the scope of the claim broadly including polypeptides with an enormous number of modifications. The scope of the claim must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a method of producing xanthan composition comprising a population of xanthan molecules having certain molecular length and increased viscosity relative to the xanthan produced by wild-type strain, wherein said method comprises selectively increasing the amount of any variant or mutant gene product of

gumB and *gumC* by a plasmid comprising said genes but not genes encoding *orfX* or *gumD, E, F* and *G* in any strain of *Xanthomonas campestris* culture and precipitating said high viscosity xanthan preparation, is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claims 5 and 39-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 5 and 39-58, as interpreted, are directed to a genus polypeptides of *gumB* and *gumC* i.e., a method of producing xanthan composition comprising a population of xanthan molecules having certain molecular length and increased viscosity relative to the xanthan produced by wild-type strain, wherein said method comprises selectively increasing the amount of any variant or mutant gene product of *gumB* and *gumC* by a plasmid comprising said genes but not genes encoding *orfX* or *gumD, E, F* and *G* in any strain of *Xanthomonas campestris* culture and precipitating said high viscosity xanthan preparation.

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it

from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In the instant case, there is no structure correlated to associated function recited in claims with regard to a methods, of producing xanthan using the members of the genus polypeptides of *gumB* and *gumC* having no structural limitations.

Due to the fact that the specification only discloses the structure of an enzymatically active the structure of an enzymatically active wild-type gene product of *gumB* and *gumC* (wild-type gene accession # *gumB: XCC2454* and wild-type *gumC* gene accession # *XCC2453*, page 8, Table 1 of specification) in a method for producing xanthan, and the lack of description of any additional species/variants/mutants from any source by any relevant, identifying characteristics or properties, one of skill in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5, 39-42 and 48-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hassler et al., (1990) and in view of Becker et al., (1998). Hassler et al., teach a set of mutants of *Xanthomonas campestris* defective in the xanthan biosynthetic pathway, which are capable of producing variant xanthans, which have rheological properties that are different from wild-type xanthan. Said reference also teaches that one could achieve altered forms of xanthans in specifically tailored mutants of *Xanthomonas campestris*, wherein alterations in the acetylation or pyruvylation or elimination of certain sugar residues in xanthans have major effects on the molecular length, viscosity and polymerization (Abstract section and Entire document). Hassler et al., also teach production and purification of xanthans. Hassler et al., is silent on the details of specific genes of the pathway that could be altered to achieve the production of xanthan with desired properties. Becker et al., have laid out the biochemical assignments for all the genes involved in the xanthan biosynthetic pathway in *Xanthomonas campestris*, i.e., the sequential reactions that take place in an orderly manner to synthesize xanthan and the gene order in the xanthan operon/genetic loci (Entire document, especially Fig.

2, page 147; Fig. 3, page 148). Specifically the reference teaches that gene products of *gumB* and *gumC* are involved in the terminal stages of xanthan biosynthesis and regulate the xanthan export and polymerization of the molecule. Said reference also suggests that elimination of unwanted by-products by genetic modifications of production strains may simplify the recovery of xanthan from the fermentation liquid (Perspectives section, page 150). It would have been obvious to a person of ordinary skill in the art to combine the teachings of Hassler et al., and Becker et al., to produce a xanthan of desired molecular length and viscosity by selectively increasing the amount of gene product of *gumB* and *gumC* by introducing additional copies of *gumB* and *gumC* genes into xanthan producing *Xanthomonas campestris*. Motivation to do so derives from the fact that improved and cost effective methods for synthesis of xanthan molecules having certain molecular length and increased viscosity to be used as an additive in the production of number of beneficial compounds in food and pharmaceutical industry. The expectation of success is high, because Hassler et al., and Becker et al., teach the effective use of genetic engineering approaches and the role of specific genes/gene loci in the xanthan biosynthetic pathway. Therefore, claims are rejected under 35 U.S.C. 103(a) as being unpatentable over Hassler et al., (1990) and in view of Becker et al., (1998).

Claims 43-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Hassler et al., (1990) and Becker et al., (1998) and further in view of Katzen et al., (1998). The combination of Hassler et al., (1990) and Becker et al., (1998) is described above. Said combination does not specifically teach an extrachromosomal element in the form of a plasmid comprising the *gumB* and *gumC* genes that can be used to generate stable integrants in a host cell i. e., *Xanthomonas campestris*. However, the use of plasmids to alter gene expression

was well known in the art. For example, Katzen et al., teach methods for generation of *Xanthomonas campestris* mutants and the effects of a combination of certain *gum* and non-*gum* gene mutations, using plasmids (episomal/extrachromosomal or plasmids capable of integrating into genome of the host) comprising one or more copies of desired xanthan biosynthetic pathway genes (Results section, column 2, page 1608; and entire document). It would have been obvious to a person of ordinary skill in the art to combine the teachings of Hassler et al., (1990) and Becker et al., (1998) and Katzen et al., (1998) to use plasmids comprising one or more copies of *gumB* and *gumC*. Motivation to do so derives from the fact, that plasmids are an easy way to increase protein expression. The expectation of success is high, because the use of plasmids for protein expression was well known, as taught by Katzen et al.,. Therefore, claims 43-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hassler et al., (1990), Becker et al., (1998) and further in view of Katzen et al., (1998).

Claim 47 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Hassler et al., (1990), Becker et al., (1998), Katzen et al., (1998) and further in view of Feinbaum R (1998). The combination of Hassler et al., (1990), Becker et al., (1998) and Katzen et al., (1998) is described above. Said combination does not specifically teach a plasmid comprising the *gumB* and *gumC* genes under the control of an inducible promoter. Feinbaum R teaches the structure and method of incorporation of inducible promoters into various plasmid constructs and the regulation of gene of interest expression via the inducible promoters through chemical and physical means. It would have been obvious to a person of ordinary skill in the art to combine the teachings of Hassler et al., (1990), Becker et al., (1998), Katzen et al., (1998) and Feinbaum R (1998) to use plasmids comprising one or more copies of desired xanthan

biosynthetic pathway genes under the control of inducible promoter. Motivation to do so derives from the fact, that an inducible promoter precisely controls the expression of the gene of interest as opposed to a constitutive promoter wherein the gene of interest is constantly in the "on" mode, which in certain cases could be toxic to the host cell. In addition, an inducible promoter gives a handle to control the expression of gene of interest depending on experimental needs: for example, during specific cell-cycle phase or following the addition of certain factors/supplements that can be converted by the polypeptides of expressed genes to yield products with defined characteristics. The expectation of success is high, because Feinbaum R teaches the structure of inducible promoters, the method of incorporation of inducible promoters into various plasmid constructs and the regulation of expression of the gene of interest via the inducible promoters through chemical and physical means. Therefore, claim 47 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hassler et al., (1990), Becker et al., (1998), Katzen et al., (1998) and further in view of Feinbaum R (1998).

The above references render claims 5 and 39-58 *prima facie* obvious to one of ordinary skill in the art.

Allowable Subject Matter/Conclusion

None of the claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached on M-F; 8:00-4:30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Feb. 08, 2007.

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